

Microbiological Associates Inc.
4733 Bethesda Avenue
Bethesda, Maryland 20014

Smoke Inhalation Carcinogenesis Study in Mice.

This contract, first of all, is to provide facilities, by renovation, new construction and provision of new equipment, for an extensive study of tobacco smoke inhalation by contrasting strains of mice, under carefully controlled and reproducible conditions, over prolonged periods.

It also provides for completing preliminary studies in preparation for the initiation of long-term experiments.

Such preliminary studies include the following:

CTR 1.1. To determine the amounts of benzo[a]pyrene (B-a-P) which, introduced directly into the lungs of the most susceptible mouse strain (principally the C3H) in various conditions and in various media (such as adsorption on iron oxide) and in several dosage sequences, may induce squamous cell carcinoma of the lung. About 23 experimental groups are contemplated and the observations are to continue as long as any mice survive, to determine the possible appearance of lung cancers or other pathological changes.

CTR 1.2. To collaborate with and assist personnel of the Process and Instruments Corp. in the development of animal holders to be used in such smoke inhalation experiments. These must not only hold the mice in such a way as to facilitate smoke inhalation, but must produce minimal stress, permit rapid and easy placement of mice and allow rapid and efficient cleaning and sterilization.

CTR 1.3. Collaborative studies will be undertaken with the Oak Ridge National Laboratory for determining actual smoke dosage and retention following exposures in the Walton and Process and Instruments Corp. smoke inhalation devices. Exposures of mice of several strains will be carried out at Microbiological Associates and the tissues sent to Oak Ridge for analysis.

CTR 1.4. Collaborative studies will be carried out with Dr. Walter B. Essman, Professor of Psychology and Biochemistry, Queens College, Flushing, N.Y. to measure, pharmacologically, the susceptibilities of various mouse strains to stress, their ability to adapt and the relative stress effects of different types of holding devices. Such determinations are essential since animals, unlike man, inhale smoke under stressful conditions so that the effects of stress may contribute significantly to the overall effects of smoke inhalation experiments.

CTR 1.5. A variety of exposure times and smoke concentrations will be used to determine acute and chronic responses to smokes from reference cigarettes of several types. The effects upon induction of aryl hydrocarbon hydroxylase will be measured.

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CTR 1.6. Effects of intratracheal "priming" doses of iron oxide, benzo[a]pyrene and methylcholanthrene administered before or during smoke inhalation will be studied to determine whether inhaled smoke has a "promoter" effect. As many as six groups of experiments, with controls, will be undertaken.

The studies listed are planned for the first part of the contract year while the physical facilities for the more extensive smoke exposure experiments are being completed. At some time during the latter part of the year, extensive experiments on cigarette smoke exposure of mice with contrasting susceptibilities to known carcinogens will be begun.

Activation Date: July 1, 1974

Current Contract Level: \$836,143.

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